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TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No. PU9990

In Re Application Of: **Song Shi, et al.**

Serial No.	Filing Date	Examiner	Group Art Unit
09/439,889	November 12, 1999	David M. Naff	1651

Invention: **Macroporous Media for Biological Application**

TO THE COMMISSIONER FOR PATENTS:

Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on **January 7, 2004.**

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Dated: **March 5, 2004**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	09/439,889	Confirmation No.: 2251
Applicant	:	Song Shi, et al.	
Filed	:	November 12, 1999	
TC/A.U.	:	1651	
Examiner	:	David M. Naff	
Docket No.	:	PU9990	
Customer No.	:	22840	

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Alexandria, Virginia 22313-1450

March 5, 2004

APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief in triplicate, appealing from the October 6, 2003, rejection of the Primary Examiner, finally rejecting claims 1, 2, 6, 8 and 9 in the captioned application. The Notice of Appeal was filed on January 7, 2004. Appellant submits, concurrently herewith, a Request for Oral Hearing in connection with the instant appeal.

REAL PARTY IN INTEREST

Amersham Biosciences AB, formerly known as Amersham Pharmacia Biotech AB, owner of the captioned application, is the real party in interest to this appeal.

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to the instant appeal.

STATUS OF CLAIMS

Claims 1, 2, 6, 8 and 9 are pending in the captioned application. These claims were amended to place them in form for appeal in an Amendment filed January 5, 2004. The claims, as amended, are reproduced in Appendix A, attached hereto.

STATUS OF AMENDMENTS

The Amendment mailed January 5, 2004 was received by the Patent Office on January 7, 2004, and is was entered by the Examiner.

SUMMARY OF INVENTION

The invention relates to the improvement of arrays of porous polymer pads on a solid support used in biological assays and the methodology for making such support. The invention involves freeze drying the porous polymer pads to increase the pore size, resulting in an enhanced ability of the porous polymer pads to bind specific substances such as nucleic acids and polypeptides.

Claims are directed to the method for making arrays of such oligonucleotides attached to the porous polymer pads (claims 1, 2 and 6) and arrays produced by such methodology (claims 8 and 9).

ISSUES

1. Whether claim 2 is properly rejected under 35 U.S.C. § 112, second paragraph.
2. Whether claims 1, 2, 6, 8 and 9 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Guschin et al or Khrapko et al (5,552,270) or Chetverin et al (5,616,478) in view of Funk et al (5,973,014), and if necessary in further view of Ruchel (1978) or Ruchel (1975) or Blank et al...

GROUPING OF CLAIMS

All of the rejected claims in the rejection appealed hereunder stand or fall together.

ARGUMENTS

1. Claim 2 is not properly rejected under 35 U.S.C. § 112, second paragraph.

The Examiner has rejected claim 2 under 35 U.S.C. § 112, second paragraph as "unclear by not having antecedently basis in claim 1 for freeze-dried array produced by the method of claim 1" continuing, "claim 1 does not require conditions that will result in freeze drying".

In response, Appellants respectfully disagree and note that claim 1 recites that a "frozen array" is produced in (b), and that this frozen array is dried in (c). Appellants respectfully assert that this unambiguously provides the antecedent basis for the freeze drying.

The Examiner also objects to the recitation in claim 2 of "specific substance" noting that "claim 1 does not require the 'specific substance' to be present in the method.

In response, Appellants respectfully point out that the language of claim 2 clearly recites that the claimed array of gel pads is prepared according to the method of claim 1 and that the specific substance is bound to each of such pads on the array. Appellants fail to see how the Examiner believes that the specific substance is required to be in the recitation of claim 1, as claim 2 neither refers back to claim 1 for antecedent basis for this

recitation, nor does it use the article "the" in referring to it; claim 2 is the first recitation of this term, which is presented as "**a** specific substance" [emphasis added].

In view of the foregoing, Appellants respectfully submit that the Examiner's rejection cannot be upheld and should be reversed.

2. Claims 1, 2, 6, 8 and 9 are not properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Guschin et al or Khrapko et al (5,552,270) or Chetverin et al (5,616,478) in view of Funk et al (5,973,014), and if necessary in further view of Ruchel (1978) or Ruchel (1975) or Blank et al...

The Examiner has rejected claims 1, 2, 6, 8 and 9 under 35 U.S.C. § 103(a) as "being unpatentable over Guschin et al or Khrapko et al (5,552,270) or Chetverin et al (5,616,478) in view of Funk et al (5,973,014), and if necessary in further view of Ruchel (1978) or Ruchel (1975) or Blank et al..."

Specifically, the Examiner states, "the claims are drawn to a method of producing an oligonucleotide array by providing an array of porous polymer gel pads on the surface of a solid support, adding an oligonucleotide probe to each of the porous pads, freezing the array of porous pads containing the oligonucleotide probe, and drying the array of porous polymer pads for a time sufficient to obtain porous polymer pads having increased

pore size. Also claimed is an oligonucleotide array of freeze-dried porous polymer gel pads on a solid support prepared by the method of claim 1".

The Examiner continues, "Guschin et al disclose drying an array of micromatrices of polyacrylamide gel pads on a support for use in immobilizing a compound such oligonucleotide..." He continues, "Khrapko et al...and Chetverin et al...disclose providing an array of porous polymer gel pads containing an oligonucleotide on the surface of a solid support and then drying the array of porous polymer gel pads on the surface. Chetverin et al disclose the polymer gel being lyophilized or dried in vacuo..."

The Examiner further states, "Funk et al disclose freeze drying swollen, non-porous, hydrophilic polymers to obtain porous, hydrophilic, highly swellable polymers having a desired pore size and pore distribution..., and which retain their original shape...Monomers used to prepare the polymer can be amides of acids such as acrylic acid...The amount of water in the swollen polymer being freeze dried can be used to control the pore size of the freeze dried polymer...". He continues, "Ruchel (1978), Ruchel (1975) and Blank et al disclose freeze drying polyacrylamide gels to obtain porous polyacrylamide polymers".

The Examiner concludes, "it would have been obvious to carry out the drying of the array of polymer gel pads on the support of Guschin et al or Khrapko et al or Chetverin et al by freeze drying to obtain the function of freeze drying to produce a porous, highly swellable polymer of a controlled desired pore size and pore distribution

as disclosed by Funk et al. It would have been expected that freeze drying can be used to increase the pore size since Funk et al disclose using the amount of water in the swollen polymer freeze dried to obtain a desired pore size. Adding an oligonucleotide probe to the pads would have been obvious since Guschin et al, Khrapko et al and Chetverin et al add an oligonucleotide to the pads. Selecting a DNA or RNA probe would have been a matter of choice depending on the use intended. The further disclosure of Ruchel (1978), Ruchel (1975) or Blank et al of freeze drying a polymer gel to obtain a porous polymer, if needed, would have further suggested carrying out the drying of Guschin et al, Khrapko et al or Chetverin et al by freeze drying. Ruchel (1978), in particular, discloses that freeze drying produces a sponge like structure without gel matrix shrinkage..."

In response, Appellants pointed out that Guschin, et al. teaches methods for making an array on porous gels. However, the reference does not disclose methods for increasing gel porous size. Likewise, Khrapko, et al. teaches methods for making arrays on polymer gels but also fails to disclose methods for increasing the pore size.

Chetverin, et al. teaches a method for entrapping components of an amplification system in a porous gel. While Appellants conceded that the reference teaches methodology of freeze-drying, it is noted that this is for the purpose of removing components that interfere with the enzymes and substrates of the amplification reaction, and not for the purpose of increasing pore sizes of gel.

Ruchel (1978) and Ruchel (1975) describe methods of freeze-drying to preserve the ultra structure of polyacrylamide gels. However, there is no teaching or suggestion in the reference that freeze-drying can be used for the purpose of increasing pore size of polyacrylamide gels. Blank, et al. describes the use of freeze-dried organic gels as crystal growth media. However, Appellants asserted that there was no teaching or even any suggestion that increased pore size permits diffusion of target molecules into gels for detection by oligonucleotide probes. Appellants submitted that the Examiner failed to make a *prima facie* case of obviousness, since none of the references, alone or in combination with each other, disclose all of the elements of the claimed invention.

In response the Examiner stated, "Applicant's arguments...have been fully considered but they are not persuasive". The Examiner concedes that Guschin et al, Khrapko et al and Chetverin et al do not disclose freeze drying to increase pore size. However, the Examiner states that these references "disclose drying porous polymer gels, and Chetverin et al discloses lyophilizing...which is freezing drying".

The Examiner continues, "since Funk et al disclose freeze drying a polymer gel to obtain a porous polymer gel having a desired controlled pore size and distribution, and the polymer freeze-dried is of the type dried by Guschin et al, Khrapko et al or Chetverin et al, it would have been obvious to freeze-dry the polymer gel of Guschin et al, Khrapko et al or Chetverin et al to obtain the result of a controlled pore size and distribution as suggested by Funk et al".

The Examiner further states, "Applicants urge that Blank et al and Ruchel (1975) and (1978) do not teach that freeze-drying will increase pore size. However, these references are combined with the Funk et al patent which suggests that freeze-drying can be used to increase pore size".

In discussing the motivation of combining Funk, et al. with the cited references, the Examiner states, "the motivation is to obtain in Guschin et al, Khrapko et al or Chetverin et al the function of freeze-drying when used to dry a polymer gel as disclosed by Funk et al, i.e. to obtain the result of producing a dried polymer gel having a controlled pore size and pore distribution..." The Examiner continues, "obviously, controlling pore size and distribution when drying in Guschin et al, Khrapko et al or Chetverin et al would have been expected to an advantage since each reference is drying a porous polymer gel. Furthermore, when freeze-drying the polymer gel of Guschin et al, Khrapko et al or Chetverin et al, a larger pore size will inherently be obtained as compared to using other methods of drying. In the present invention, the pore size increase is with respect to drying methods other than freeze-drying since the improvement as disclosed in the specification is using freeze-drying in place of known drying methods".

In response, Appellants urge that the Examiner is misapplying the teachings of the cited references. Specifically, the Guschin, et al. and Khrapko, et al. references do not teach freeze-drying the gel. The Guschin teaches microchips with three-dimensional gel pads to achieve a greater binding capacity for oligonucleotide probes than conventional

two-dimensional glass supports. While Guschin, et al. does teach drying of these pads, such drying is not for increasing the pore size of the gel but rather, to make the gels amenable to storage. The Khrapko, et al. reference teaches oligonucleotide gel arrays and the plurality of mechanically spaced dots to localize the oligonucleotides within a specified gel volume. There is no teaching or suggestion of freeze-drying this gel to increase pore size.

While the Chetverin, et al. reference does, as the Examiner states, discuss lyophilization of the gels before soaking with enzymes, there is no teaching nor any suggestion that nucleic acids are bound to the gel during the lyophilization, nor is there any teaching of arrays.

Likewise, the Blank, et al. and Ruchel references teach freeze-drying of polyacrylamide gels but none of these references disclose or even suggests freeze-drying gels for binding assays, particularly with binding substances attached.

The Funk, et al. reference provides a process for the appropriation of porous hydrophilic and a highly swellable hydrogels using freeze-drying techniques to achieve "desired pore size" or the desired pore size distribution. However, Funk, et al. neither teaches nor suggests the use of such porous hydrogels in binding assays to a specific substances such as polynucloetides, nor does it teach freeze-drying of an array containing oligonucleotide probes.

Further, while Appellants are mindful that the Examiner has stated that the motivation to combine the foregoing references is to use the freeze-drying disclosed by Funk, et al. to obtain "a dry polymer gel having a controlled pore size and pore distribution", there is no disclosure nor even any suggestion, in any of these references that the arrays contained oligonucleotides can be freeze-dried to result in increased pore size. Indeed, Appellants respectfully assert that such is only attainable through the teachings of Appellants own application.

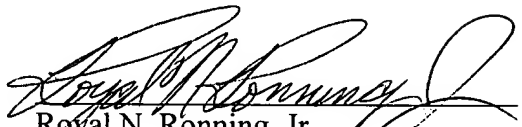
Appellants further respectfully assert that such is not a proper basis upon which to base an obviousness rejection. Specifically, the only teaching that shows arrays containing oligonucleotides on gel pads can be freeze-dried to result in increased pore size is the teachings of Appellants own application. The references themselves certainly provide no cogent teachings that could be relied upon to show this. Indeed, the only reference which shows that pore size could be increased is the Funk, et al. reference, which neither discloses nor even suggests arrays or oligonucleotide arrays.

In view of the foregoing, Appellants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness, and, as such, the rejection cannot be upheld and should be reversed.

CONCLUSION

In view of the foregoing, Appellants respectfully assert that the Examiner's rejections presented above cannot be sustained, and should be reversed.

Respectfully submitted,



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APPENDIX A

The Rejected Claims

Claim 1 (previously presented): A method of making an oligonucleotide array comprising:

a. providing an array of porous polymer gel pads on the surface of a solid support;

b. adding an oligonucleotide probe to each of said porous polymer gel pads;

c. freezing said array of porous polymer gel pads comprising said oligonucleotide probes to produce a frozen array; and

d. drying said frozen array of porous polymer gel pads for a time sufficient to increase the pore size of each of said porous polymer gel pads.

Claim 2 (previously presented): An oligonucleotide array of freeze-dried porous polymer gel pads on a solid support, comprising a specific substance bound to each of the porous polymer gel pads, prepared using the steps of claim 1.

Claims 3–5 (cancelled)

Claim 6 (previously presented): The method of claim 1 wherein said freezing is at liquid nitrogen temperatures and said drying is by sublimation.

Claim 7 (cancelled)

Claim 8 (previously presented): An array produced by the method of claim 1, wherein said oligonucleotide probe is a DNA probe.

Claim 9 (previously presented): An array produced by the method of claim 1, wherein said oligonucleotide probe is an RNA probe.